Measles Vaccine and Inflammatory Bowel Disease (IBD)

Q & A

At a glance: There is strong scientific evidence to show that measles vaccine does not cause inflammatory bowel disease (IBD). CDC recognizes there is considerable public interest in this issue, and therefore supports additional research regarding this hypothesis. CDC is committed to maintaining the safest, most effective vaccine supply in history.

What is Inflammatory Bowel Disease (IBD)?

Inflammatory Bowel Disease, also known as IBD, is a general medical term used to refer to chronic inflammatory diseases of the intestine.

Two common inflammatory bowel diseases are ulcerative colitis and Crohn's disease. These chronic illnesses can inflame the gastrointestinal tract causing bloody diarrhea, abdominal pain, and weight loss. Ulcerative colitis can affect the entire large intestine or the rectum. Crohn's disease mainly affects short segments of both the small and large intestine. Although IBD can begin at any age, it's usual onset is from age 15 to 30 years. IBD is a rare disease with 3-20 new cases recognized per 100,000 persons per year.

What causes inflammatory bowel disease?

The cause(s) of inflammatory bowel disease is not known.

There are several unproven theories as to the cause(s) of IBD:

1. IBD is known to "run in families" suggesting a possible inherited, or genetic cause.

2. A possible environmental cause is suggested because Crohn's disease most often occurs in people who smoke, are residents of Northern European countries and live in urban areas.

3. Another theory is that significant emotional events in a persons life may trigger the disease.

4. Other researchers speculate that the disease may be caused by an infection or virus.

5. Still others believe that the body's immune system is reacting to unidentified or unknown antigens. This antigen would cause the immune system to respond inappropriately against normal intestinal tissue, resulting in chronic inflammation.

Measles, mumps or rubella virus infection is not known cause IBD. The virus that causes measles disease infects the respiratory system and then spreads to lymphatic tissue (an important part of our immune system). During the acute infection, lymph cells in the gastrointestinal (GI) tract are infected but whether this causes chronic inflammation is

highly questionable. One theory speculates that measles virus may persist in the intestine in certain individuals and later trigger a chronic inflammatory infection, however this has not been proven. Because MMR vaccine contains a very weak live measles virus it has been suggested that measles vaccine could cause an inflammatory process in the intestine. This theory has not been proven and is speculative. Two types of scientific data - epidemiological and pathological - can be studied to look at a possible link between measles infection and IBD. However, because conflicting results have been obtained for both types of data by different investigators, this link can not be established.

What about studies that suggest an association between measles vaccine and IBD?

The possibility of an association between measles virus and chronic inflammatory bowel disease was discussed in a 1998 study by Wakefield and colleagues. The researchers believed they discovered a new childhood illness that caused bowel disease and psychiatric problems including behavioral disorders and autism. MMR vaccine was suggested as a possible cause. The theory is that MMR vaccine could lead to intestinal inflammation resulting in decreased absorption by the intestinal tract of essential vitamins and nutrients which in turn could lead to developmental disorders. An editorial expressing concerns about the study was also published in the same issue (Chen 1998). That all patients in the study had bowel disease is not surprising since all were referred to a department of gastroenterology. Some of the concerns expressed were that in this small study (12 patients) there is no report of detection of vaccine viruses in intestinal or brain tissue for any of the patients. Multiple laboratories using more sensitive and specific tests, have failed to detect any findings to suggest this. In addition, the GI pathology should have existed prior to the behavioral symptoms to support their theory. The researchers reported the onset of GI symptoms was unknown in 5 patients and noted that GI problems occurred after the onset of behavioral symptoms in another 5 patients. Two Swedish studies have also suggested a high risk of Crohn's Disease in those exposed to measles in utero. However, these studies involved very small numbers of cases, 2 cases in the first study and 4 in the second study, 2 of which were cases in the first study (Ekbom et al 1994, Ekbom et al 1996).

In 1995, researchers (Thompson et al.) suggested in a retrospective cohort study that MMR vaccine might be a risk factor for Crohn's disease. However, the selection and recall biases and the differences in data collection in this study were so substantial as to cast doubt on the validity of the findings.

Another study has reported finding measles virus proteins and RNA in the intestinal tissue of cases of Crohn's disease using in situ hybridization and immunologic staining (Wakefield 1993). However, the validity of this finding was later called into question when it could not be reproduced by other researchers (see question #4).

In 2002, researchers (Uhlmann et al., 2002) found measles virus fragments in the intestines of children with "new variant" IBD (children with both IBD and developmental disorder). Scientists looked for the presence of measles virus in the intestinal tissue of 91 children with new variant IBD and 70 "controls" (children without this type of IBD). The

researchers found measles virus fragments in 75 out of the 91 children with IBD, and in only 5 of the 70 controls. While this provides evidence for an association between the presence of measles virus and IBD in children with developmental disorder, it does not mean that natural measles virus or the measles component of the MMR vaccine causes IBD or developmental disorder. A commentary published with the article asserts that the data could just as easily be interpreted as indicating that the IBD or the developmental disorder cause the persistence of measles in the intestines (Morris & Aldulaimi, 2002). In addition, the researchers did not compare the virus found in the intestines of patients with the virus used in the vaccine; nor did they provide information regarding whether or not the children in the study had been previously vaccinated with MMR or had previously contracted measles disease. The limitations of this study are further discussed in a letter written by the Director of CDC's National Immunization Program to the UK's Chief Medical Officer.

Is there scientific evidence to show there is no association between measles vaccine and IBD?

There is strong scientific evidence (both epidemiological and laboratory) to show there is no association between measles vaccine and inflammatory bowel disease.
A population-based study conducted by the CDC in collaboration with four large HMO's, part of the Vaccine Safety Datalink Project, concluded that there was no evidence that vaccination with MMR or other measles-containing vaccines, or the the age of vaccination early in life, was associated with an increased risk for the the development of IBD (Davis et al, 2001). Using a case-control design, the study compared patients diagnosed with IBD and those without IBD, and looked at the vaccination history of MMR vaccine and the timing of vaccinations. Vaccination with MMR or other measles-containing vaccines, or the timing of vaccination early in life, did not increase the risk for IBD.

Researchers in the UK (Frombonne & Chakrabarti, 2001) conducted a study to test the idea that a new form, or "new variant," of Inflammatory Bowel Disease (IBD) exists which is a combination of developmental regression and gastrointestinal symptoms occurring shortly after MMR immunization. Information on 96 children (95 immunized with MMR) who were born between 1992 and 1995 and were diagnosed with pervasive developmental disorder were compared with data from 2 groups of autistic patients (one group of 98 born before MMR was ever used and one group of 68 who were likely to have received MMR vaccine). No evidence was found to support a new syndrome of MMR-induced autism. For instance, the researchers found that there were no differences between vaccinated and unvaccinated groups with regard to when their parents first became concerned about their child's development. Similarly, the rate of developmental regression reported in the vaccinated and unvaccinated groups was not different; therefore, there was no suggestion that developmental regression had increased in frequency since MMR was introduced. Of the 96 children in the first group, no inflammatory bowel disorder was reported.

Another group of researchers in the UK (Taylor et al., 2002) also examined whether MMR vaccination is associated with bowel problems and developmental regression in children with autism, looking for evidence of a "new variant" form of IBD/autism. The study included 278 cases of children with autism and 195 with atypical autism (cases with many of the features of childhood autism but not quite meeting the required criteria for that diagnosis, or with atypical features such as onset of symptoms after the age of 3 years). The cases included in this study were born between 1979 and 1998. The proportion of children with developmental regression or bowel symptoms did not change significantly from 1979 to 1988, a period which included the introduction of MMR vaccination in the UK in 1988. No significant difference was found in rates of bowel problems or regression in children who received the MMR vaccine before their parents became concerned about their development, compared with those who received it only after such concern and those who had not received the MMR vaccine. The findings provide no support for an MMR associated "new variant" form of autism and further evidence against involvement of MMR vaccine in the initiation of autism.

Four other epidemiologic studies have failed to confirm the possible association between measles virus and inflammatory bowel disease. Nielsen et al. (1998) examined all possible cases of measles in pregnant women admitted to a Copenhagen hospital from 1915-1966. None of the offspring of the 25 identified women had developed Crohn's disease. In their case-control studies, Jones et al (1997) and Feeney et al (1997) found no association between IBD and measles infection or measles vaccine, respectively. In 1995, Hermon-Taylor compared the incidence of Crohn's disease in England and Wales with measles infection, including information after the introduction of measles vaccine. No association was found.

In another study, researchers used the same laboratory methodology as Wakefield et al. (1993), and could not identify any measles virus in patients with IBD, although they did find the presence of other viral and bacterial agents (Liu et al., 1995). Several other research groups using more sensitive and specific tests (polymerase chain reaction, PCR) have not found any evidence of measles virus RNA in the gastrointestinal tissues of patients with Crohn's Disease or ulcerative colitis (Haga 1996, Iizuka 1995, Afzal 1998).

What does CDC recommend for measles-mumps-rubella (MMR) vaccine?

The CDC continues to recommend two doses of MMR vaccine for all persons; for children, the first dose is recommended at 12-15 months of age and the second dose is recommended at 4-6 years of age. MMR vaccine protects children against dangerous, even deadly, diseases. For instance, one out of 30 children with measles gets pneumonia. For every 1,000 children who get the disease, one or two will die from it. Thanks to vaccines, we have few cases of measles in the U.S. today. However, the disease is extremely contagious and each year dozens of cases are imported from abroad into the U.S., threatening the health of people who have not been vaccinated and those for whom the vaccine was not effective.

Although the risk of Inflammatory Bowel Disease (IBD) is higher for those who have relatives with IBD, there are no data to suggest that measles vaccine will increase or decrease this risk. Measles vaccine is recommended for children with a family history of IBD unless there is another specific reason not to vaccinate (for example, in persons who are very ill and are not able to fight infections).

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